Annals of Clinical and Analytical Medicine
Original Research

The role of monocyte to HDL-cholesterol ratio and neutrophil to lymphocyte ratio in metabolic syndrome

Inflammatory markers in metabolic syndrome

Serkan Karahan, Ertugrul Okuyan
Department of Cardiology, Health Sciences University, Bağcılar Training and Research Hospital, İstanbul, Turkey

Abstract
Aim: Metabolic syndrome (MetS) is characterized by a low-grade inflammatory condition that causes changes in noninvasive indices, namely the monocyte-to-high-density lipoprotein (HDL) ratio (MHR) and neutrophil-to-lymphocyte ratio (NLR), from which blood counts are derived. In our study, we aimed to evaluate systemic inflammatory markers in cases of MetS.
Material and Methods: A retrospective analysis of a population of 156 subjects (88 control subjects and 68 MetS patients) was performed in this study. Patients followed in our hospital with the diagnosis of MetS between June 2018 and June 2021 were included in the study. Demographic data of the patients, such as age and gender, and vital signs, lipid profiles, and complete blood count results at admission were recorded and analyzed.
Results: There were statistically significant differences between the MetS group and the control group in terms of age, gender, fasting blood glucose, hemoglobin, HDL, low-density lipoprotein (LDL), total cholesterol, triglycerides, white blood cell count, lymphocytes, and monocytes (p=0.008, p=0.024, p=0.001, p=0.022, p=0.034, p=0.001, p=0.001, p=0.001, p=0.001, and p=0.001, respectively). While the NLR was statistically significantly lower in the MetS group compared to the control group (p=0.001), the MHR was statistically significantly higher in the MetS group (p=0.001). There was a significant positive correlation between MetS and male gender, age, fasting blood glucose, white blood cell count, lymphocytes, monocytes, HDL, LDL, total cholesterol, triglycerides, MHR, and survival status. There was a significant negative correlation between MetS and NLR. There was a statistically significant difference in survival between the MetS group and the control group (p=0.019). Of all the patients included in this study, 16 (30.2%) patients in the MetS group and 9 (12.3%) in the control group died. The MHR was higher among deceased patients than survivors (p=0.001).
Discussion: The MHR and NLR, which are inexpensive markers that can be calculated easily in all centers, can be used in the evaluation of MetS and mortality.

Keywords
Metabolic Syndrome, Monocyte-to-HDL Ratio, Neutrophil-to-Lymphocyte Ratio, Mortality

DOI: 10.4328/ACAM.20776 Received: 2021-07-08 Accepted: 2021-08-20 Published Online: 2021-09-07 Printed: 2021-12-01 Ann Clin Anal Med 2021;12(12):1397-1400
Corresponding Author: Serkan Karahan, Department of Cardiology, Health Sciences University, Bağcılar Training and Research Hospital, 34200, İstanbul, Turkey.
E-mail: drserkankarahan@gmail.com P: +90 532 159 44 01
Corresponding Author ORCID ID: https://orcid.org/0000-0002-1203-7615

Introduction

Metabolic syndrome (MetS) is a systemic condition characterized by a wide range of clinical features such as central obesity, hypertension, and impaired glucose and lipid homeostasis [1]. Various changes have been made to the definition of MetS over the last 20 years. In 2006, the International Diabetes Federation established some criteria to define MetS. These are fasting plasma glucose of ≥100 mg/dL (or drug therapy for high glucose), high-density lipoprotein (HDL) concentration of <40 mg/dL in men or <50 mg/dL in women (or drug therapy for dyslipidemia), triglycerides of ≥150 mg/dL (or drug therapy for high triglycerides), waist circumference of >94 cm in men or >80 cm in women, and systolic arterial pressure of ≥130 mmHg or diastolic blood pressure of ≥85 mmHg (or antihypertensive therapy) [2].

MetS is characterized by a low-grade inflammatory state caused by increased cytokine, chemokine, and adipokine production and abnormal activation of immune cells that collectively contribute to atherosclerotic plaque formation and non-alcoholic fatty liver disease [3, 4].

Recently, subtypes of leukocyte ratios (neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and monocyte-to-HDL ratio (MHR)) have been recognized as markers of systemic inflammation [5]. In addition, various studies have stated that there are relationships between NLR, PLR, LMR, MHR, and cardiovascular diseases such as peripheral arterial occlusive disease, coronary artery diseases (including myocardial infarction), atrial fibrillation, and aortic changes, but the relationship with MetS is still not fully established [6-8]. HDL cholesterol, on the other hand, abolishes the proinflammatory and pro-oxidant effects of monocytes by inhibiting the migration of macrophages. Therefore, MHR may indicate a patient's inflammatory state [9]. Previous studies have indicated that MHR may be a new cardiovascular prognostic marker [1-4, 10].

In our study, we aimed to evaluate systemic inflammatory markers in cases of MetS.

Material and Methods

This study was designed as a retrospective cohort study. Before the start of the study, the study protocol was approved by the local ethics committee of Medipol University hospital and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki. A retrospective analysis of a population of 156 subjects (88 control subjects and 68 MetS patients) was performed. Patients followed in our hospital with the diagnosis of MetS between June 2018 and June 2021 were included in the study. Patient files were scanned through the hospital registry system, and patient data were retrospectively scanned and recorded.

Demographic data such as age and gender, vital signs, complete blood count results at admission (hemoglobin, neutrophils, platelets, lymphocytes, monocytes), lipid profiles (triglycerides, HDL, LDL), and smoking status were recorded and analyzed. Correlations of the NLR and the MHR with MetS were analyzed.

Statistical Analysis

The data obtained in this study were analyzed using the statistical program SPSS 25 (IBM Corp., Armonk, NY, USA). Descriptive statistics such as frequency distribution, mean, and standard deviation were used to evaluate the data. The difference between the means of two independent groups was compared with the Student t-test. The Mann-Whitney U test, which is a nonparametric alternative to that test, was used when parametric test assumptions were not met. Descriptive statistics were expressed with odds ratios and 95% confidence intervals (Cis). Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off point, the area under the curve (AUC), the sensitivity, and the specificity of the data. Categorical data were analyzed with chi-square or Fisher exact tests. Values of $p<0.05$ were considered statistically significant at the 95% CI.

Results

There were statistically significant differences between the MetS group and the control group in terms of age, gender, fasting blood glucose, hemoglobin, HDL, LDL, total cholesterol, triglycerides, white blood cell count, lymphocytes, and monocytes (p=0.008, p=0.024, p=0.001, p=0.022, p=0.034, p=0.001, p=0.001, p=0.001, p=0.001, and p=0.001, respectively) (Table 1). While the NLR was statistically significantly lower in the MetS group compared to the control group (p=0.001), the MHR was statistically significantly higher in the MetS group (p=0.001) (Table 1).

Table 1. Comparison of patients' sociodemographic, clinical, and laboratory parameters

Parameters	Control (n=73)	Metabolic syndrome (n=53)	p
	Mean±SD (min-max), n (%)	Mean±SD (min-max), n (%)	
Age (years)	61.73±13.6 (31-87)	68.23±13.0 (34-91)	0.008*
Gender			
Male	41 (56.2%)	19 (64.2%)	0.024*
Female	32 (43.8%)	34 (35.8)	
Smoking habit	20 (27.7%)	16 (30.2%)	0.735*
Fasting blood sugar (mg/dL)	103.96±11.8 (89-160)	184.40±51.9 (89.0-346.0)	0.001
Hemoglobin (g/dL)	12.30±2.1 (7.5-17.0)	11.51±1.8 (8.1-16.0)	0.022
HDL (mg/dL)	42.56±11.2 (18.0-74.0)	35.57±11.6 (20.0-79.0)	0.034*
LDL (mg/dL)	84.99±26.3 (50.0-122.0)	136.06±41.6 (50.0-252.0)	0.001
Total cholesterol (mg/dL)	151.98±25.3 (118.0-199.0)	211.09±52.0 (106.2-338.0)	0.001
Triglycerides (mg/dL)	97.80±26.4 (61.0-155.0)	160.17±62.9 (48.0-331.0)	0.001
Albumin (g/dL)	3.40±0.5 (1.7-4.6)	3.41±0.6 (2.1-4.8)	0.233*
Leukocytes (103/μL)	6.44±2.3 (1.0-12.7)	12.48±1.0 (4.8-45.7)	0.001
Neutrophils (109/L)	6.70±1.8 (4.5-10.5)	7.85±5.8 (0.1-32.3)	0.128
Lymphocytes (109/L)	1.21±0.4 (0.4-2.9)	3.75±5.2 (0.3-25.0)	0.001
Platelets (109/L)	230.0±93.9 (95.0-521.0)	230.1±100.0 (4.7-497.0)	0.990*
Monocytes (109/L)	0.47±0.20 (0.0-1.1)	1.09±1.5 (0.0-9.4)	0.001
Neutrophil/lymphocyte ratio	6.54±3.4 (1.8-17.5)	4.52±5.7 (0.0-28.6)	0.001
Monocyte-to-HDL ratio	0.012±0.00 (0.0-0.04)	0.029±0.04 (0.0-0.3)	0.001
Survival status			
Survivor	64 (87.7%)	37 (69.8%)	0.019*
Deceased	9 (12.3%)	16 (30.2%)	

*: Student t-test was used. HDL: High-density lipoprotein, LDL: low-density lipoprotein.

There was a statistically significant difference in survival between the MetS group and the control group (p=0.019) (Table 1). Of all patients included in this study, 16 (30.2%) patients in the MetS group and 9 (12.3%) in the control group died. The MHR was higher among deceased patients than survivors (p=0.001) (Table 1).

There was a significant positive correlation between MetS and male gender, age, fasting blood glucose, leukocytes, lymphocytes, monocytes, HDL, LDL, total cholesterol, triglycerides, MHR, and survival status. There was a significant negative correlation between MetS and NLR (Table 2).

According to ROC analysis, MHR (AUC: 0.746, 95% CI: 0.655-0.836, p=0.001) and NLR (AUC: 0.23, 95% CI: 0.138-0.333, p=0.001) were prognostic factors for MetS (Figure 1).

Of all patients included in this study, 16 (30.2%) patients in the MetS group and 9 (12.3%) in the control group died. The MHR was higher among deceased patients (0.041±0.01) than survivors (0.023±0.07) (p=0.001) (Figure 2).

Table 2. Correlation analysis between metabolic syndrome and other variables

	Correlation coefficient (r)	p
Male gender	0.423**	0.000
Age	0.461**	0.000
Fasting blood sugar	0.525**	0.008
Neutrophils	0.436**	0.018
Lymphocytes	0.360**	0.023
Monocytes	0.753**	0.000
HDL	0.704**	0.002
LDL	0.407**	0.000
Total cholesterol	0.498**	0.000
Triglycerides	0.357**	0.000
MHR	0.772**	0.004
Survival status	0.680**	0.025
NLR	-0.607**	0.010

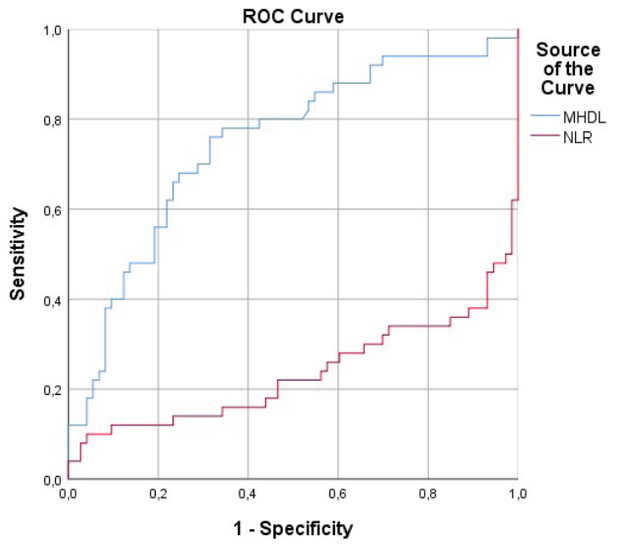

Figure 1. ROC analysis of MHR and NLR in patients with MetS

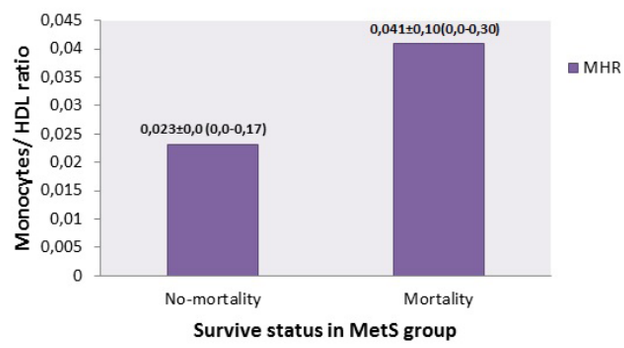

Figure 2. Relationship between survival status and MHR

Discussion

In this study, we investigated the relationships of the obtained laboratory markers of MHR and NLR with MetS. MetS is a disease with significant morbidity and mortality, characterized by various risk factors such as central obesity, dyslipidemia, hypertension, hyperglycemia, and low-grade inflammatory state. Several studies have highlighted the role of inflammation in the development of MetS and atherosclerosis. The literature also suggests that the analysis of parameters that can be easily measured from peripheral complete blood count, such as NLR and MHR, could be useful in evaluating the chronic inflammatory state seen in MetS patients.

Inflammation is the most commonly suggested mechanism to explain the relationship between MetS and hematological parameters. Inflammation plays a primary role in the pathophysiology of MetS. In inflammatory diseases, the number of monocytes increases and HDL cholesterol levels decrease. Monocytes are a different type of leukocytes and they migrate to tissue macrophages and initiate inflammation. In previous studies, it was reported that the number of monocytes was associated with the prediction of coronary artery disease [11]. On the other hand, HDL cholesterol inhibits the activation of monocytes, inhibits the conversion of monocytes into macrophages, and reduces inflammation. Thus, the combination of these two parameters in the MHR is thought to represent inflammatory processes. This relationship between monocytes and HDL cholesterol has prompted researchers to investigate whether MHR is more effective than monocyte count or HDL cholesterol alone in predicting cardiovascular events. Kanbay et al. reported that MHR acts as an independent predictor for cardiovascular events and increases in parallel with the decrease in estimated glomerular filtration rate in patients with chronic kidney disease [12]. It has been suggested that MHR is associated with systemic infection and endothelial dysfunction and can be used as a new inflammation-based diagnostic and prognostic marker in cardiovascular diseases. In the study by Pamukcu and Aker, the MHR was associated with calcification of the mitral annulus [13]. Yilmaz et al. reported that in the follow-up of patients with angina pectoris who had undergone percutaneous coronary bare-metal stent implantation, high values of preintervention MHR were found to be closely associated with in-stent restenosis [14]. In addition, another recent study demonstrated a significant and independent association between MHR and saphenous vein graft disease in patients undergoing coronary bypass graft surgery [15]. In our study, the MHR was found to be statistically significantly higher in the MetS group compared to the control group and significant

positive correlations were found between MetS and male gender, age, fasting blood glucose, leukocytes, lymphocytes, monocytes, HDL, LDL, total cholesterol, triglycerides, MHR, and survival status. In ROC analysis, MHR was found to be a prognostic factor for MetS. In addition, 16 patients (30.2%) in the MetS group and 9 (12.3%) in the control group died among all patients included in this study. The MHR was higher among the deceased patients (0.041±0.01) than the survivors (0.023±0.07).

The NLR has also been proposed as a surrogate marker for inflammation in different populations and it has prognostic and predictive value [1, 4, 10, 16]. Yue et al. reported the predictive value of the NLR in cases of diabetic retinopathy [17]. Additionally, in a study involving cases of acute pulmonary embolism, low NLR was found to be an independent predictor of in-hospital and short-term mortality [18]. NLR was also observed to be associated with vascular pathologies such as coronary artery and peripheral vascular diseases [19]. In another study, it was demonstrated that there was a significant negative correlation between coronary slow flow and NLR value [20]. In our study, the NLR was statistically significantly lower in the MetS group compared to the control group while there was a significant negative correlation between MetS and NLR. In ROC analysis, the NLR was found to be a prognostic factor for MetS.

This study has some limitations. It was designed as an observational, retrospective, and single-center study. In addition, repeating the MHR and NLR measurements at regular intervals would likely affect the results. We were unable to compare the MHR and NLR with other markers used in cases of MetS. More extensive studies are needed to further elucidate these relationships.

Conclusion

We suggest that the MHR and NLR, as inexpensive markers that can be easily calculated in all centers, can be used in the evaluation of MetS and mortality. The results of our study should be supported by multicenter and larger patient groups.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: *None*

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Vahit D, Akboga MK, Samet Y, Huseyin E. Assessment of monocyte to high density lipoprotein cholesterol ratio and lymphocyte-to-monocyte ratio in patients with metabolic syndrome. Biomark Med. 2017;11(7):535-40.

2. Abaci A, Kilickap M, Goksuluk H, Karaaslan D, Barcin C, Kayikcioglu M, et al. [Data on prevalence of metabolic syndrome in Turkey: Systematic review, meta-analysis and meta-regression of epidemiological studies on cardiovascular risk factors]. Turk Kardiyol Dern Ars. 2018;46(7):591-601.

3. Al Saudi RM, Kasabri V, Naffa R, Bulatova N, Bustanji Y. Glycated LDL-C and glycated HDL-C in association with adiposity, blood and atherogenicity indices in metabolic syndrome patients with and without prediabetes. Ther Adv Endocrinol Metab. 2018;9(10):311-23.

4. Battaglia S, Scialpi N, Berardi E, Antonica G, Suppressa P, Diella FA, et al. Gender, BMI and fasting hyperglycaemia influence Monocyte to-HDL ratio (MHR) index in metabolic subjects. PLoS One. 2020;15(4):e0231927.

5. Karahan S, Okuyan E. Systemic Inflammatory Index and Platelet-to-Lymphocyte Ratio Predicted Mortality in patients with Acute Myocardial Infarction. Experimental Applied Medical Science. 2021;2(2):146-53.

6. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014;35(43):3033-69, 69a-69k.

7. Alper S, Ulu MS, Kazan S, Tunca O, Kazan ED. Comparison Of Monocyte/HDL Ratio In Routine Hemodialysis And Peritoneal Dialysis Patients. Dicle Tıp Dergisi. 2020;47(1):139-7.

8. Marongiu F, Mameli A, Grandone E, Barcellona D. Pulmonary Thrombosis: A Clinical Pathological Entity Distinct from Pulmonary Embolism? Semin Thromb Hemost. 2019;45(8):778-83.

9. Varol S, Karahan S, Okuyan E. Monocyte High-Density Lipoprotein cholesterol Ratio and coronary collateral circulation development in patients with stable coronary artery disease and no history of revascularization. The Medical Journal Of Haydarpaşa Numune Training Research Hospital. 2021;63(2):0-.

10. Jialal I, Jialal G, Adams-Huet B, Ramakrishnan N. Neutrophil and monocyte ratios to high-density lipoprotein-cholesterol and adiponectin as biomarkers of nascent metabolic syndrome. Horm Mol Biol Clin Investig. 2020;41(2).

11. Zeynalova S, Bucksch K, Scholz M, Yahiaoui-Doktor M, Gross M, Loffler M, et al. Monocyte subtype counts are associated with 10-year cardiovascular disease risk as determined by the Framingham Risk Score among subjects of the LIFE-Adult study. PLoS One. 2021;16(3):e0247480.

12. Kanbay M, Solak Y, Unal HU, Kurt YG, Gok M, Cetinkaya H, et al. Monocyte count/HDL cholesterol ratio and cardiovascular events in patients with chronic kidney disease. Int Urol Nephrol. 2014;46(8):1619-25.

13. Pamukcu HE, Aker M. Association between monocyte to HDL cholesterol ratio and mitral annulus calcification. Journal of Surgery Medicine. 2019;3(1):44-8.

14. Yilmaz S, Akboga MK, Sen F, Balci KG, Aras D, Temizhan A, et al. Usefulness of the monocyte-to-high-density lipoprotein cholesterol ratio to predict bare metal stent restenosis. Biomark Med. 2016;10(9):959-66.

15. Akboga MK, Yayla C, Balci KG, Ozeke O, Maden O, Kisacik H, et al. Relationship between Serum Albumin Level and Monocyte-to-High-Density Lipoprotein Cholesterol Ratio with Saphenous Vein Graft Disease in Coronary Bypass. Thorac Cardiovasc Surg. 2017;65(4):315-21.

16. Sefil F, Ulutas KT, Dokuyucu R, Sumbul AT, Yengil E, Yagiz AE, et al. Investigation of neutrophil lymphocyte ratio and blood glucose regulation in patients with type 2 diabetes mellitus. J Int Med Res. 2014;42(2):581-8.

17. Yue S, Zhang J, Wu J, Teng W, Liu L, Chen L. Use of the Monocyte-to-Lymphocyte Ratio to Predict Diabetic Retinopathy. Int J Environ Res Public Health. 2015;12(8):10009-19.

18. Ertem AG, Yayla C, Acar B, Kirbas O, Unal S, Uzel Sener M, et al. Relation between lymphocyte to monocyte ratio and short-term mortality in patients with acute pulmonary embolism. Clin Respir J. 2018;12(2):580-6.

19. Gary T, Pichler M, Belaj K, Eller P, Hafner F, Gerger A, et al. Lymphocyte-to-monocyte ratio: a novel marker for critical limb ischemia in PAOD patients. Int J Clin Pract. 2014;68(12):1483-7.

20. Yayla C, Akboga MK, Gayretli Yayla K, Ertem AG, Efe TH, Sen F, et al. A novel marker of inflammation in patients with slow coronary flow: lymphocyte-to-monocyte ratio. Biomark Med. 2016;10(5):485-93.

How to cite this article:

Serkan Karahan, Ertugrul Okuyan. *Evaluation of systemic inflammatory markers in metabolic syndrome. Ann Clin Anal Med 2021;12(12):1397-1400*